



033072-092.ST25

SEQUENCE LISTING

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Eckhardt, Allen E.

<120> Methods of Identifying Reduced Internalization
Transmembrane Receptor Agonists

<130> 033072-092

<140> US 10/693,164

<141> 2003-10-24

<150> US 60/421,538

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<223> amino acid motif

<221> VARIANT

<222> 3, 4

<223> Xaa = Any Amino Acid

<400> 1

Asn Pro Xaa Xaa Tyr
1 5

<210> 2

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<222> 4

<223> Xaa = Any Amino Acid

<400> 2

Cys Ala Ala Xaa
1

<210> 3

<211> 43

<212> PRT
 <213> Homo sapiens

<400> 3
 Asn Pro Ile Val Tyr Ala Phe Arg Ile Gln Lys Phe Arg Val Thr Phe
 1 5 10 15
 Leu Lys Ile Trp Asn Asp His Phe Arg Cys Gln Pro Ala Pro Pro Ile
 20 25 30
 Asp Glu Asp Leu Pro Glu Glu Arg Pro Asp Asp
 35 40

<210> 4
 <211> 176
 <212> PRT
 <213> Homo sapiens

<400> 4
 Asn Pro Ile Ile Tyr Pro Cys Ser Ser Lys Glu Phe Arg Ala Phe Val
 1 5 10 15
 Arg Ile Leu Gly Cys Gln Cys Arg Gly Arg Gly Arg Arg Arg Arg
 20 25 30
 Arg Arg Arg Arg Leu Gly Gly Cys Ala Tyr Thr Tyr Arg Pro Trp Thr
 35 40 45
 Arg Gly Gly Ser Leu Glu Arg Ser Gln Ser Arg Lys Asp Ser Leu Asp
 50 55 60
 Asp Ser Gly Ser Cys Leu Ser Gly Ser Gln Arg Thr Leu Pro Ser Ala
 65 70 75 80
 Ser Pro Ser Pro Gly Tyr Leu Gly Arg Gly Ala Pro Pro Pro Val Glu
 85 90 95
 Leu Cys Ala Phe Pro Glu Trp Lys Ala Pro Gly Ala Leu Leu Ser Leu
 100 105 110
 Pro Ala Pro Glu Pro Pro Gly Arg Arg Gly Arg His Asp Ser Gly Pro
 115 120 125
 Leu Phe Thr Phe Lys Leu Leu Thr Glu Pro Glu Ser Pro Gly Thr Asp
 130 135 140
 Gly Gly Ala Ser Asn Gly Gly Cys Glu Ala Ala Asp Val Ala Asn
 145 150 155 160
 Gly Gln Pro Gly Phe Lys Ser Asn Met Pro Leu Ala Pro Gly Gln Phe
 165 170 175

<210> 5
 <211> 29
 <212> PRT
 <213> Homo sapiens

<400> 5
 Asn Pro Val Ile Tyr Thr Ile Phe Asn His Asp Phe Arg Arg Ala Phe
 1 5 10 15
 Lys Lys Ile Leu Cys Arg Gly Asp Arg Lys Arg Ile Val
 20 25

<210> 6
 <211> 29
 <212> PRT
 <213> Homo sapiens

<400> 6

Asn	Pro	Val	Ile	Tyr	Thr	Ile	Phe	Asn	Gln	Asp	Phe	Arg	Arg	Ala	Phe
1				5					10					15	
Arg	Arg	Ile	Leu	Cys	Arg	Pro	Trp	Thr	Gln	Thr	Ala	Trp			
			20					25							

<210> 7

<211> 31

<212> PRT

<213> Homo sapiens

<400> 7

Asn	Pro	Val	Ile	Tyr	Thr	Val	Phe	Asn	Gln	Asp	Phe	Arg	Pro	Ser	Phe
1				5					10					15	
Lys	His	Ile	Leu	Phe	Arg	Arg	Arg	Arg	Arg	Arg	Gly	Phe	Arg	Gln	
			20					25					30		

<210> 8

<211> 105

<212> PRT

<213> Homo sapiens

<400> 8

Asn	Pro	Ile	Ile	Tyr	Cys	Arg	Ser	Pro	Asp	Phe	Arg	Lys	Ala	Phe	Gln
1				5					10					15	
Gly	Leu	Leu	Cys	Cys	Ala	Arg	Arg	Ala	Ala	Arg	Arg	Arg	His	Ala	Thr
			20					25					30		
His	Gly	Asp	Arg	Pro	Arg	Ala	Ser	Gly	Cys	Leu	Ala	Arg	Pro	Gly	Pro
		35					40					45			
Pro	Pro	Ser	Pro	Gly	Ala	Ala	Ser	Asp	Asp	Asp	Asp	Asp	Asp	Val	Val
		50				55				60					
Gly	Ala	Thr	Pro	Pro	Ala	Arg	Leu	Leu	Glu	Pro	Trp	Ala	Gly	Cys	Asn
65					70				75					80	
Gly	Gly	Ala	Ala	Ala	Asp	Ser	Asp	Ser	Ser	Leu	Asp	Glu	Pro	Cys	Arg
				85				90						95	
Pro	Gly	Phe	Ala	Ser	Glu	Ser	Lys	Val							
			100					105							

<210> 9

<211> 92

<212> PRT

<213> Homo sapiens

<400> 9

Asn	Pro	Leu	Ile	Tyr	Cys	Arg	Ser	Pro	Asp	Phe	Arg	Ile	Ala	Phe	Gln
1				5					10					15	
Glu	Leu	Leu	Cys	Leu	Arg	Arg	Ser	Ser	Leu	Lys	Ala	Tyr	Gly	Asn	Gly
			20					25					30		
Tyr	Ser	Ser	Asn	Gly	Asn	Thr	Gly	Glu	Gln	Ser	Gly	Tyr	His	Val	Glu
		35					40					45			
Gln	Glu	Lys	Glu	Asn	Lys	Leu	Cys	Glu	Asp	Leu	Pro	Gly	Thr	Glu	
		50				55				60					
Asp	Phe	Val	Gly	His	Gln	Gly	Thr	Val	Pro	Ser	Asp	Asn	Ile	Asp	Ser
65					70				75					80	
Gln	Gly	Arg	Asn	Cys	Ser	Thr	Asn	Asp	Ser	Leu	Leu				
				85				90							

<210> 10
 <211> 120
 <212> PRT
 <213> Homo sapiens

<400> 10
 Asn Pro Ile Ile Tyr Ala Phe Asn Ala Asp Phe Arg Lys Ala Phe Ser
 1 5 10 15
 Thr Leu Leu Gly Cys Tyr Arg Leu Cys Pro Ala Thr Asn Asn Ala Ile
 20 25 30
 Glu Thr Val Ser Ile Asn Asn Asn Gly Ala Ala Met Phe Ser Ser His
 35 40 45
 His Glu Pro Arg Gly Ser Ile Ser Lys Glu Cys Asn Leu Val Tyr Leu
 50 55 60
 Ile Pro His Ala Val Gly Ser Ser Glu Asp Leu Lys Lys Glu Glu Ala
 65 70 75 80
 Ala Gly Ile Ala Arg Pro Leu Glu Lys Leu Ser Pro Ala Leu Ser Val
 85 90 95
 Ile Leu Asp Tyr Asp Thr Asp Val Ser Leu Glu Lys Ile Gln Pro Ile
 100 105 110
 Thr Gln Asn Gly Gln His Pro Thr
 115 120

<210> 11
 <211> 22
 <212> PRT
 <213> Homo sapiens

<400> 11
 Asn Pro Ile Ile Tyr Thr Thr Phe Asn Ile Glu Phe Arg Lys Ala Phe
 1 5 10 15
 Leu Lys Ile Leu His Cys
 20

<210> 12
 <211> 22
 <212> PRT
 <213> Homo sapiens

<400> 12
 Asn Pro Val Ile Tyr Thr Thr Phe Asn Ile Glu Phe Arg Lys Ala Phe
 1 5 10 15
 Leu Lys Ile Leu Ser Cys
 20

<210> 13
 <211> 24
 <212> PRT
 <213> Homo sapiens

<400> 13
 Asn Pro Val Ile Tyr Thr Val Phe Asn Ala Glu Phe Arg Asn Val Phe
 1 5 10 15
 Arg Lys Ala Leu Arg Ala Cys Cys
 20

<210> 14
 <211> 123
 <212> PRT
 <213> Homo sapiens

<400> 14
 Asn Pro Val Ile Tyr Ala Phe Asn Ala Asp Phe Gln Lys Val Phe Ala
 1 5 10 15
 Gln Leu Leu Gly Cys Ser His Phe Cys Ser Arg Thr Pro Val Glu Thr
 20 25 30
 Val Asn Ile Ser Asn Glu Leu Ile Ser Tyr Asn Gln Asp Ile Val Phe
 35 40 45
 His Lys Glu Ile Ala Ala Ala Tyr Ile His Met Met Pro Asn Ala Val
 50 55 60
 Thr Pro Gly Asn Arg Glu Val Asp Asn Asp Glu Glu Glu Gly Pro Phe
 65 70 75 80
 Asp Arg Met Phe Gln Ile Tyr Gln Thr Ser Pro Asp Gly Asp Pro Val
 85 90 95
 Ala Glu Ser Val Trp Glu Leu Asp Cys Glu Gly Glu Ile Ser Leu Asp
 100 105 110
 Lys Ile Thr Pro Phe Thr Pro Asn Gly Phe His
 115 120

<210> 15
 <211> 47
 <212> PRT
 <213> Homo sapiens

<400> 15
 Asn Pro Met Cys Tyr Ala Leu Cys Asn Lys Ala Phe Arg Asp Thr Phe
 1 5 10 15
 Arg Leu Leu Leu Leu Cys Arg Trp Asp Lys Arg Arg Trp Arg Lys Ile
 20 25 30
 Pro Lys Arg Pro Gly Ser Val His Arg Thr Pro Ser Arg Gln Cys
 35 40 45

<210> 16
 <211> 31
 <212> PRT
 <213> Homo sapiens

<400> 16
 Asn Pro Ala Cys Tyr Ala Leu Cys Asn Ala Thr Phe Lys Lys Thr Phe
 1 5 10 15
 Lys His Leu Leu Met Cys His Tyr Lys Asn Ile Gly Ala Thr Arg
 20 25 30

<210> 17
 <211> 51
 <212> PRT
 <213> Homo sapiens

<400> 17
 Asn Pro Val Cys Tyr Ala Leu Cys Asn Lys Thr Phe Arg Thr Thr Phe
 1 5 10 15

Lys Met Leu Leu Leu Cys Gln Cys Asp Lys Lys Lys Arg Arg Lys Gln
 20 25 30
 Gln Tyr Gln Gln Arg Gln Ser Val Ile Phe His Lys Arg Ala Pro Glu
 35 40 45
 Gln Ala Leu
 50

<210> 18
 <211> 31
 <212> PRT
 <213> Homo sapiens

<400> 18
 Asn Pro Ala Cys Tyr Ala Leu Cys Asn Ala Thr Phe Lys Lys Thr Phe
 1 5 10 15
 Arg His Leu Leu Leu Cys Gln Tyr Arg Asn Ile Gly Thr Ala Arg
 20 25 30

<210> 19
 <211> 42
 <212> PRT
 <213> Homo sapiens

<400> 19
 Asn Pro Ile Cys Tyr Ala Leu Cys Asn Arg Thr Phe Arg Lys Thr Phe
 1 5 10 15
 Lys Met Leu Leu Leu Cys Arg Trp Lys Lys Lys Val Glu Glu Lys
 20 25 30
 Leu Tyr Trp Gln Gly Asn Ser Lys Leu Pro
 35 40

<210> 20
 <211> 24
 <212> PRT
 <213> Homo sapiens

<400> 20
 Asn Pro Val Ile Tyr Ala Tyr Phe Asn Lys Asp Phe Gln Asn Ala Phe
 1 5 10 15
 Lys Lys Ile Ile Lys Cys Lys Phe
 20

<210> 21
 <211> 26
 <212> PRT
 <213> Homo sapiens

<400> 21
 Asn Pro Ile Ile Tyr Thr Met Ser Asn Glu Asp Phe Lys Gln Ala Phe
 1 5 10 15
 His Lys Leu Ile Arg Phe Lys Cys Thr Ser
 20 25

<210> 22

<211> 24
 <212> PRT
 <213> Homo sapiens

<400> 22
 Asn Pro Leu Leu Tyr Thr Ser Phe Asn Glu Asp Phe Lys Leu Ala Phe
 1 5 10 15
 Lys Lys Leu Ile Arg Cys Arg Glu
 20

<210> 23
 <211> 37
 <212> PRT
 <213> Homo sapiens

<400> 23
 Asn Pro Ile Ile Tyr Cys Leu Arg Asn Gln Glu Val Lys Arg Ala Leu
 1 5 10 15
 Cys Cys Ile Leu His Leu Tyr Gln His Gln Asp Pro Asp Pro Lys Lys
 20 25 30
 Gly Ser Arg Asn Val
 35

<210> 24
 <211> 27
 <212> PRT
 <213> Homo sapiens

<400> 24
 Asn Pro Leu Ile Tyr Thr Leu Arg Asn Met Glu Val Lys Gly Ala Leu
 1 5 10 15
 Arg Arg Leu Leu Gly Lys Gly Arg Glu Val Gly
 20 25

<210> 25
 <211> 62
 <212> PRT
 <213> Homo sapiens

<400> 25
 Asn Pro Leu Phe Tyr Gly Phe Leu Gly Lys Lys Phe Lys Arg Tyr Phe
 1 5 10 15
 Leu Gln Leu Leu Lys Tyr Ile Pro Pro Lys Ala Lys Ser His Ser Asn
 20 25 30
 Leu Ser Thr Lys Met Ser Thr Leu Ser Tyr Arg Pro Ser Asp Asn Val
 35 40 45
 Ser Ser Ser Thr Lys Lys Pro Ala Pro Cys Phe Glu Val Glu
 50 55 60

<210> 26
 <211> 50
 <212> PRT
 <213> Homo sapiens

<400> 26

Asn Pro Phe Leu Tyr Cys Phe Val Gly Asn Arg Phe Gln Gln Lys Leu
 1 5 10 15
 Arg Ser Val Phe Arg Val Pro Ile Thr Trp Leu Gln Gly Lys Arg Glu
 20 25 30
 Ser Met Ser Cys Arg Lys Ser Ser Ser Leu Arg Glu Met Glu Thr Phe
 35 40 45
 Val Ser
 50

<210> 27
 <211> 51
 <212> PRT
 <213> Homo sapiens

<400> 27
 Asn Pro Leu Ile Tyr Ala Phe Ile Gly Gln Lys Phe Arg His Gly Leu
 1 5 10 15
 Leu Lys Ile Leu Ala Ile His Gly Leu Ile Ser Lys Asp Ser Leu Pro
 20 25 30
 Lys Asp Ser Arg Pro Ser Phe Val Gly Ser Ser Ser Gly His Thr Ser
 35 40 45
 Thr Thr Leu
 50

<210> 28
 <211> 67
 <212> PRT
 <213> Homo sapiens

<400> 28
 Asn Pro Leu Ile Tyr Ala Phe Ala Gly Glu Lys Phe Arg Arg Tyr Leu
 1 5 10 15
 Tyr His Leu Tyr Gly Lys Cys Leu Ala Val Leu Cys Gly Arg Ser Val
 20 25 30
 His Val Asp Phe Ser Ser Ser Glu Ser Gln Arg Ser Arg His Gly Ser
 35 40 45
 Val Leu Ser Ser Asn Phe Thr Tyr His Thr Ser Asp Gly Asp Ala Leu
 50 55 60
 Leu Leu Leu
 65

<210> 29
 <211> 59
 <212> PRT
 <213> Homo sapiens

<400> 29
 Asn Pro Ile Leu Tyr Asn Leu Val Ser Ala Asn Phe Arg His Ile Phe
 1 5 10 15
 Leu Ala Thr Leu Ala Cys Leu Cys Pro Val Trp Arg Arg Arg Arg Lys
 20 25 30
 Arg Pro Ala Phe Ser Arg Lys Ala Asp Ser Val Ser Ser Asn His Thr
 35 40 45
 Leu Ser Ser Asn Ala Thr Arg Glu Thr Leu Tyr
 50 55

<210> 30
 <211> 107
 <212> PRT
 <213> Homo sapiens

<400> 30
 Asn Pro Ile Ile Tyr Cys Cys Leu Asn Asp Arg Phe Arg Leu Gly Phe
 1 5 10 15
 Lys His Ala Phe Arg Cys Cys Pro Phe Ile Ser Ala Gly Asp Tyr Glu
 20 25 30
 Gly Leu Glu Met Lys Ser Thr Arg Tyr Leu Gln Thr Gln Gly Ser Val
 35 40 45
 Tyr Lys Val Ser Arg Leu Glu Thr Thr Ile Ser Thr Val Val Gly Ala
 50 55 60
 His Glu Glu Glu Pro Glu Asp Gly Pro Lys Ala Thr Pro Ser Ser Leu
 65 70 75 80
 Asp Leu Thr Ser Asn Cys Ser Ser Arg Ser Asp Ser Lys Thr Met Thr
 85 90 95
 Glu Ser Phe Ser Phe Ser Ser Asn Val Leu Ser
 100 105

<210> 31
 <211> 50
 <212> PRT
 <213> Homo sapiens

<400> 31
 Asn Pro Trp Ile Tyr Ala Ser Phe Ser Ser Val Ser Ser Glu Leu Arg
 1 5 10 15
 Ser Leu Leu Cys Cys Ala Arg Gly Arg Thr Pro Pro Ser Leu Gly Pro
 20 25 30
 Gln Asp Glu Ser Cys Thr Thr Ala Ser Ser Ser Leu Ala Lys Asp Thr
 35 40 45
 Ser Ser
 50

<210> 32
 <211> 83
 <212> PRT
 <213> Homo sapiens

<400> 32
 Asn Pro Val Ile Tyr Asn Leu Met Ser Gln Lys Phe Arg Ala Ala Phe
 1 5 10 15
 Arg Lys Leu Cys Asn Cys Lys Gln Lys Pro Thr Glu Lys Pro Ala Asn
 20 25 30
 Tyr Ser Val Ala Leu Asn Tyr Ser Val Ile Lys Glu Ser Asp His Phe
 35 40 45
 Ser Thr Glu Leu Asp Asp Ile Thr Val Thr Asp Thr Tyr Leu Ser Ala
 50 55 60
 Thr Lys Val Ser Phe Asp Asp Thr Cys Leu Ala Ser Glu Val Ser Phe
 65 70 75 80
 Ser Gln Ser

<210> 33

<211> 65
 <212> PRT
 <213> Homo sapiens

<400> 33
 Asn Pro Trp Ile Tyr Met Leu Phe Thr Gly His Leu Phe His Glu Leu
 1 5 10 15
 Val Gln Arg Phe Leu Cys Cys Ser Ala Ser Tyr Leu Lys Gly Arg Arg
 20 25 30
 Leu Gly Glu Thr Ser Ala Ser Lys Ser Asn Ser Ser Ser Phe Val
 35 40 45
 Leu Ser His Arg Ser Ser Ser Gln Arg Ser Cys Ser Gln Pro Ser Thr
 50 55 60
 Ala
 65

<210> 34
 <211> 75
 <212> PRT
 <213> Homo sapiens

<400> 34
 Asn Pro Val Leu Tyr Ser Leu Met Ser Ser Arg Phe Arg Glu Thr Phe
 1 5 10 15
 Gln Glu Ala Leu Cys Leu Gly Ala Cys Cys His Arg Leu Arg Pro Arg
 20 25 30
 His Ser Ser His Ser Leu Ser Arg Met Thr Thr Gly Ser Thr Leu Cys
 35 40 45
 Asp Val Gly Ser Leu Gly Ser Trp Val His Pro Leu Ala Gly Asn Asp
 50 55 60
 Gly Pro Glu Ala Gln Gln Glu Thr Asp Pro Ser
 65 70 75

<210> 35
 <211> 62
 <212> PRT
 <213> Homo sapiens

<400> 35
 Asn Pro Leu Val Tyr Cys Phe Met His Arg Arg Phe Arg Gln Ala Cys
 1 5 10 15
 Leu Glu Thr Cys Ala Arg Cys Cys Pro Arg Pro Pro Arg Ala Arg Pro
 20 25 30
 Arg Ala Leu Pro Asp Glu Asp Pro Pro Thr Pro Ser Ile Ala Ser Leu
 35 40 45
 Ser Arg Leu Ser Tyr Thr Thr Ile Ser Thr Leu Gly Pro Gly
 50 55 60

<210> 36
 <211> 82
 <212> PRT
 <213> Homo sapiens

<400> 36
 Asn Pro Leu Val Tyr Ala Leu Ala Ser Arg His Phe Arg Ala Arg Phe
 1 5 10 15

Arg Arg Leu Trp Pro Cys Gly Arg Arg Arg Arg His Arg Ala Arg Arg
 20 25 30
 Ala Leu Arg Arg Val Arg Pro Ala Ser Ser Gly Pro Pro Gly Cys Pro
 35 40 45
 Gly Asp Ala Arg Pro Ser Gly Arg Leu Leu Ala Gly Gly Gly Gln Gly
 50 55 60
 Pro Glu Pro Arg Glu Gly Pro Val His Gly Gly Glu Ala Ala Arg Gly
 65 70 75 80
 Pro Glu

<210> 37
 <211> 76
 <212> PRT
 <213> Homo sapiens

<400> 37
 Asn Pro Ile Ile Tyr Thr Leu Thr Asn Lys Glu Met Arg Arg Ala Phe
 1 5 10 15
 Ile Arg Ile Met Ser Cys Cys Lys Cys Pro Ser Gly Asp Ser Ala Gly
 20 25 30
 Lys Phe Lys Arg Pro Ile Ile Ala Gly Met Glu Phe Ser Arg Ser Lys
 35 40 45
 Ser Asp Asn Ser Ser His Pro Gln Lys Asp Glu Gly Asp Asn Pro Glu
 50 55 60
 Thr Ile Met Ser Ser Gly Asn Val Asn Ser Ser Ser
 65 70 75

<210> 38
 <211> 80
 <212> PRT
 <213> Homo sapiens

<400> 38
 Asn Pro Ile Ile Tyr Ala Leu Arg Ser Lys Asp Leu Arg His Ala Phe
 1 5 10 15
 Arg Ser Met Phe Pro Ser Cys Glu Gly Thr Ala Gln Pro Leu Asp Asn
 20 25 30
 Ser Met Gly Asp Ser Asp Cys Leu His Lys His Ala Asn Asn Ala Ala
 35 40 45
 Ser Val His Arg Ala Ala Glu Ser Cys Ile Lys Ser Thr Val Lys Ile
 50 55 60
 Ala Lys Val Thr Met Ser Val Ser Thr Asp Thr Ser Ala Glu Ala Leu
 65 70 75 80

<210> 39
 <211> 59
 <212> PRT
 <213> Homo sapiens

<400> 39
 Asn Pro Val Leu Tyr Ala Phe Leu Asp Glu Asn Phe Lys Arg Cys Phe
 1 5 10 15
 Arg Gln Leu Cys Arg Lys Pro Cys Gly Arg Pro Asp Pro Ser Ser Phe
 20 25 30
 Ser Arg Pro Arg Glu Ala Thr Ala Arg Glu Arg Val Thr Ala Cys Thr

35 40 45
Pro Ser Asp Gly Pro Gly Gly Gly Arg Ala Ala
50 55

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<210> 40
<211> 58
<212> PRT
<213> Homo sapiens
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<400> 40
Asp Pro Phe Val Tyr Tyr Phe Val Ser His Asp Phe Arg Asp His Ala
 1          5          10          15
Lys Asn Ala Leu Leu Cys Arg Ser Val Arg Thr Val Lys Gln Met Gln
 20          25          30
Val Ser Leu Thr Ser Lys Lys His Ser Arg Lys Ser Ser Ser Tyr Ser
 35          40          45
Ser Ser Ser Thr Thr Val Lys Thr Ser Tyr
 50          55

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<210> 41
<211> 66
<212> PRT
<213> Homo sapiens
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<400> 41
Asn Gly Glu Val Gln Ala Glu Leu Arg Arg Lys Trp Arg Arg Trp His
 1           5           10           15
Leu Gln Gly Val Leu Gly Trp Ser Ser Lys Ser Gln His Pro Trp Gly
          20           25           30
Gly Ser Asn Gly Ala Thr Cys Ser Thr Gln Val Ser Met Leu Thr Arg
          35           40           45
Val Ser Pro Ser Ala Arg Arg Ser Ser Ser Phe Gln Ala Glu Val Ser
 50           55           60
Leu Val
65

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